CLAIMS

The following claims are pending in this application.

1. **(Previously Presented)** A method of selectively inhibiting expression of a mutant target allele of a gene in a cell or organism comprising wild-type and mutant alleles of the gene, wherein the target allele comprises a dominant gain of function mutation that is correlated with a disorder, the method comprising administering to the cell or organism an siRNA specific for the target allele such that allele-specific RNA interference of the mutant target allele occurs and expression of the wild-type allele is preserved.

2. **(Previously Presented)** The method of claim 1, wherein the disorder is a neurodegenerative disorder associated with a mutant protein encoded by the mutant allele, the mutant protein having a toxic property.

3. **(Previously Presented)** The method of claim 2, wherein the disorder is selected from the group of amyotrophic lateral sclerosis, Huntington's disease, Alzheimer's disease, and Parkinson's disease.

4. **(Previously Presented)** The method of claim 2, wherein the disorder is amyotrophic lateral sclerosis.

5. **(Previously Presented)** The method of claim 1, wherein the siRNA is targeted to the gain of function mutation.

6. **(Previously Presented)** The method of claim 1, wherein the siRNA is capable of single nucleotide discrimination.

7. **(Previously Presented)** The method of claim 1, wherein the mutant and wild-type alleles differ by only one, two, or three nucleotides.

8. **(Previously Presented)** The method of claim 1, wherein the mutant and wild-type alleles differ by only a single nucleotide.

9. **(Previously Presented)** A method of selectively inhibiting expression of a mutant target allele of a gene in a cell or organism comprising wild-type and mutant alleles of the gene, wherein the mutant target allele comprises a point mutation, the method comprising administering to the cell or organism an siRNA targeted to the point mutation such that allele-specific RNA interference of the mutant target allele occurs and expression of the wild-type allele is preserved.

10. **(Previously Presented)** The method of claim 9, wherein the point mutation is correlated with a dominant gain of function disorder.

11. **(Previously Presented)** The method of claim 9, where the siRNA is capable of single nucleotide discrimination.

12. **(Previously Presented)** The method of claim 9, wherein the mutant and wild-type alleles differ by one, two, or three nucleotides.

13. -27. **(Canceled)**

28. **(Previously Presented)** The method of claim 9, wherein the mutant and wild-type alleles differ by a single nucleotide.

29. **(Previously Presented)** The method of claim 1 or 9, wherein the siRNA is matched completely with a mutant mRNA encoded by the mutant allele point mutation but comprises a single nucleotide mismatch with a wild-type mRNA encoded by the wild-type allele.

30. **(Previously Presented)** The method of claim 29, wherein the mismatch is a purine:purine mismatch.

31. **(Previously Presented)** The method of claim 30, wherein the mismatch is a G:G mismatch.

32. **(Previously Presented)** The method of claim 29, wherein the single nucleotide mismatch is located at nucleotide position 10 (P10) relative to the 5' end of the antisense strand of the siRNA.

33. **(Previously Presented)** The method of claim 29, wherein the single nucleotide mismatch is located at nucleotide position 9 (P9) relative to the 5' end of the antisense strand of the siRNA.

34. **(Previously Presented)** The method of claim 10, wherein the disorder is a neurodegenerative disorder associated with a mutant protein encoded by the mutant allele, the mutant protein having a toxic property.

35. **(Previously Presented)** The method of claim 34, wherein the disorder is amyotrophic lateral sclerosis.

36. **(Previously Presented)** The method of claim 35, wherein the gene is SOD1.

37. **(Previously Presented)** The method of claim 36, wherein the mutant allele encodes a glycine to arginine mutation at amino acid position 85 (G85R) of a SOD1 protein.

38. **(Previously Presented)** The method of claim 36, wherein the mutant allele encodes a glycine to alanine mutation at amino acid position 93 (G93A) of a SOD1 protein.

39. **(Previously Presented)** The method of claim 36, wherein the siRNA comprises (i) a sense strand sequence corresponding to the sequence set forth as SEQ ID NO: 3; and (ii) an anti-sense strand sequence set forth as SEQ ID NO: 4.

40. **(Previously Presented)** The method of claim 36, wherein the siRNA comprises (i) a sense strand sequence set forth as SEQ ID NO: 1; and (ii) an anti-sense strand sequence set forth as SEQ ID NO: 2.

41. **(Previously Presented)** The method of claim 1 or 9, wherein the siRNA is administered to cell in the form of a shRNA, wherein the shRNA is cleaved in the cell to generate the siRNA.

42. **(Previously Presented)** The method of claim 41, wherein the shRNA is matched with a mutant mRNA encoded by the mutant allele and contains a single nucleotide mismatch with a wild-type mRNA encoded by the wild-type allele.

43. **(Previously Presented)** The method of claim 42, wherein the single nucleotide mismatch is located at position (P10) relative to the 5' end of the shRNA.

44. **(Previously Presented)** The method of claim 43, wherein the gene is SOD1.

45. **(Previously Presented)** The method of claim 44, wherein the shRNA is a G93A SOD1 shRNA.

46. **(Previously Presented)** The method of claim 45, wherein the G93A SOD1 shRNA has the sequence set forth as SEQ ID NO: 16.

47. **(Previously Presented)** The method of claim 41, wherein the shRNA is expressed from an expression construct.

48. **(Previously Presented)** The method of claim 47, wherein the shRNA is expressed under the control of a RNA polymerase III (U6) promoter.